In the Specification

Please substitute the following paragraph on page 13, line 7:

Also provided by the present invention is a method of producing an antibody that binds at least two different human inhibitory KIR receptor gene products, wherein said antibody is capable of neutralizing KIR-mediated inhibition of NK cell cytotoxicity in a population of NK cells expressing said at least two different human inhibitory KIR receptor gene products, said method comprising the steps of:

a) isolating from a hybridoma of the invention a nucleic acid encoding said monoclonal antibody;

b) optionally modifying said nucleic acid so as to obtain a modified nucleic acid that comprises a sequence that encodes a modified or derivatized antibody comprising an amino acid sequence that corresponds to a functional sequence of the monoclonal antibody or is substantially similar thereto (e.g., is at least about 65%, at least about 75%, at least about 85%, at least about 90%, at least about 95% (such as about 70-99%) identical to such a sequence) selected from a humanized antibody, a chimeric antibody, a single chain antibody, an immunoreactive fragment of an antibody, or a fusion ~~protien~~ protein comprising such an immunoreactive fragment;

c) inserting said nucleic acid or modified nucleic acid (or related nucleic acid coding for the same amino acid sequence) into an expression vector, wherein said encoded antibody or antibody fragment is capable of being expressed when said expression vector is present in a host cell grown under appropriate conditions;

d) transfecting a host cell with said expression vector, wherein said host cell does not otherwise produce immunoglobulin protein;

e) culturing said transfected host cell under conditions which cause the expression of said antibody or antibody fragment; and

isolating the antibody or antibody fragment produced by said transfected host cell. Preferably the antibody binds a common determinant present on KIR2DL1 and KIR2DL2/3.

Please substitute the following paragraphs on page 18, line 10:

Figure 7 depicts an epitope map showing results of competitive binding experiments obtained by surface plasmon resonance (~~BIAcore®~~BIACORE) analysis with anti-KIR antibodies to KIR2DL1, where overlapping circles designate overlap in binding to KIR2DL1. Results show that 1-7F9 is competitive with EB6 and 1-4F1, but not with NKVSF1 and DF200, on KIR 2DL1. Antibody 1-4 F1 in turn is competitive with EB6, DF200, NKVSF1, and 1-7 F9. Antibody NKVSF1 competes with DF200, 1-4F1, and EB6, but not 1-7F9, on KIR2DL1. DF200 competes with NKVSF1, 1-4F1, and EB6, but not 1-7F9, on KIR2DL1.

Figure 8 depicts an epitope map showing results of competitive binding experiments obtained by ~~BIAcore®~~ BIACORE analysis with anti-KIR antibodies to KIR2DL3, where overlapping circles designate overlap in binding to KIR2DL3. Results show that 1-4F1 is competitive with NKVSF1, DF200, gl183, and 1-7F9 on KIR2DL3. 1-7F9 is competitive with DF200, gl183, and 1-4F1, but not with NKVSF1, on KIR2DL3. NKVSF1 competes with DF200, 1-4F1, and GL183, but not 1-7F9, on KIR2DL3. DF200 competes with NKVSF1, 1-4F1, and 1-7F9, but not with GL183, on KIR2DL3.

Figure 9 depicts an epitope map showing results of competitive binding experiments obtained by ~~BIAcore®~~ BIACORE analysis with anti-KIR antibodies to KIR2DS1, where overlapping circles designate overlap in binding to KIR2DS1. Results show that antibody 1-4F1 is competitive with NKVSF1, DF200, and 1-7F9 on KIR2DS1. Antibody 1-7F9 is competitive with 1-4F1, but not competitive with DF200 and NKVSF1 on KIR2DS1. NKVSF1 competes with DF200 and 1-4F1, but not with 1-7F9, on KIR2DS1. DF200 competes with NKVSF1 and 1-4F1, but not with 1-7F9, on KIR2DS1.

Please substitute the following paragraph on page 20, line 29 to page 21, line 14:

The antibodies of this invention may be produced by a variety of techniques known in the art. Typically, they are produced by immunization of a non-human animal, preferably a mouse, with an immunogen comprising an inhibitory KIR polypeptide, preferably a KIR2DL polypeptide, more preferably a human KIR2DL polypeptide. The inhibitory KIR polypeptide may comprise the full length sequence of a human inhibitory KIR polypeptide, or a fragment or derivative thereof, typically

an immunogenic fragment, i.e., a portion of the polypeptide comprising an epitope exposed on the surface of the cell expressing an inhibitory KIR receptor. Such fragments typically contain at least about 7 consecutive amino acids of the mature polypeptide sequence, even more preferably at least about 10 consecutive amino acids thereof. Fragments typically are essentially derived from the extra-cellular domain of the receptor. Even more preferred is a human KIR2DL polypeptide which includes at least one, more preferably both, extracellular Ig domains, of the full length KIRDL polypeptide and is capable of mimicking at least one conformational epitope present in a KIR2DL receptor. In other embodiments, said polypeptide comprises at least about 8 consecutive amino acids of an extracellular Ig domain of amino acid positions 1-224 of the KIR2DL1 polypeptide (amino acid numbering of according to PROW web site describing the KIR gene family, ~~http://www.~~ See Worldwide Website: ncbi.nlm.nih.gov/prow/guide/1326018082.htm)

Please substitute the following paragraph on page 22, line 31 to page 23, line 11:

Once isolated and present in single cell suspension, the lymphocytes can be fused to an immortal cell line. This is typically a mouse myeloma cell line, although many other immortal cell lines useful for creating hybridomas are known in the art. Preferred murine myeloma lines include, but are not limited to, those derived from MOPC-21 and MPC-11 mouse tumors available from the Salk Institute Cell Distribution Center, San Diego, Calif. U.S.A., X63 Ag8653 and SP-2 cells available from the American Type Culture Collection, ~~Rockville, Maryland U.S.A~~10801 University Boulevard, Manassas, VA 20110-2209. The fusion is effected using polyethylene glycol or the like. The resulting hybridomas are then grown in selective media that contains one or more substances that inhibit the growth or survival of the unfused, parental myeloma cells. For example, if the parental myeloma cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine (HAT medium), which substances prevent the growth of HGPRT-deficient cells.

Please substitute the following paragraph on page 42, line 7:

It has been found that antibody NKVSF1 also binds to NK cells from cynomolgus monkeys, see example 7. The invention therefore provides an ~~an~~ antibody, as well as fragments and derivatives

thereof, wherein said antibody, fragment or derivative cross-reacts with at least two inhibitory human KIR receptors at the surface of human NK cells, and which furthermore binds to NK cells from cynomolgus monkeys. In one embodiment hereof, the antibody is not antibody NKVSF1. The ~~invetion~~ invention also ~~provdes~~ provides a method of testing the toxicity of an antibody, as well as fragments and derivatives thereof, wherein said antibody, fragment or derivative cross-reacts with at least two inhibitory human KIR receptors at the surface of human NK cells, wherein the method comprises testing the antibody in a cynomolgus monkey.

Please substitute the following paragraph on page 46, line 6:

Several monoclonal antibodies have been shown to be efficient in clinical situations, such as ~~Rituxan~~ RITUXAN (Rituximab), ~~Herceptin~~HERCEPTIN (Trastuzumab) or ~~Xolair~~ XOLAIR (Omalizumab), and similar administration regimens (i.e., formulations and/or doses and/or administration protocols) may be used with the antibodies of this invention. Schedules and dosages for administration of the antibody in the pharmaceutical compositions of the present invention can be determined in accordance with known methods for these products, for example using the manufacturers' instructions. For example, an antibody present in a pharmaceutical composition of this invention can be supplied at a concentration of 10 mg/mL in either 100 mg (10 mL) or 500 mg (50 mL) single-use vials. The product is formulated for IV administration in 9.0 mg/mL sodium chloride, 7.35 mg/mL sodium citrate dihydrate, 0.7 mg/mL polysorbate 80, and Sterile Water for Injection. The pH is adjusted to 6.5. An exemplary suitable dosage range for an antibody in a pharmaceutical composition of this invention may between about 10 mg/m^2 and 500 mg/m^2. However, it will be appreciated that these schedules are exemplary and that an optimal schedule and regimen can be adapted taking into account the affinity and tolerability of the particular antibody in the pharmaceutical composition that must be determined in clinical trials. Quantities and schedule of injection of an antibody in a pharmaceutical composition of this invention that saturate NK cells for 24 hours, 48 hours 72 hours or a week or a month will be determined considering the affinity of the antibody and the its pharmacokinetic parameters.

Please substitute the following paragraph on page 53, line 19:

Preferred disorders that can be treated according to the invention include hematopoietic tumors of lymphoid lineage, for example T-cell and B-cell tumors, including but not limited to T-cell disorders such as T-prolymphocytic leukemia (T-PLL), including of the small cell and cerebriform cell type; large granular lymphocyte leukemia (LGL) preferably of the T-cell type; Sezary syndrome (SS); Adult T-cell leukemia lymphoma (ATLL); a/d T-NHL hepatosplenic lymphoma; peripheral/post-thymic T cell lymphoma (pleomorphic and immunoblastic subtypes); angio immunoblastic T-cell lymphoma; angiocentric (nasal) T-cell lymphoma; anaplastic (Ki 1+) large cell lymphoma; intestinal T-cell lymphoma; T-lymphoblastic; and lymphoma/~~leukaemia~~leukemia (T-Lbly/T-ALL).

Please substitute the following paragraph on page 54, line 26:

Protozoa infections that may be treated according to this invention include, but are not limited to, infections caused by leishmania, kokzidioa, and trypanosoma. A complete list of infectious diseases can be found on the website of the National Center for Infectious Disease (NCID) at the Center for Disease Control (CDC) (~~http://www.cdc.gov/ncidod/diseases/~~See Worldwide Website: cdc.gov/ncidod/diseases/), which list is incorporated herein by reference. All of said diseases are candidates for treatment using the cross-reacting inhibitory KIR antibodies of the invention.

Please substitute the following paragraph on page 58, line 10:

F(ab')2 fragments were also tested for their ability to ~~reconstite~~ reconstitute lysis of Cw4 positive targets. F(ab')2 fragments of the DF200 and EB6 Abs were both able to reverse inhibition of lysis by KIR2DL1-transfected NK cells of the Cw4 transfected 221 cell line and the Cw4+ TUBO EBV cell line. Results are shown in Figure 4.

Please substitute the following paragraphs on page 60, line 19:

For kinetic measurements, various concentrations of the soluble antibody (1×10^{-7} to 4×10^{-10} M) were applied onto the immobilized sample. Measurements were performed at a 20 µl/min continuous flow rate. For each cycle, the surface of the sensor chip was regenerated by 5 µl injection of 10 mM NaOH pH 11. The ~~BIAlogue~~ BIALOGUE Kinetics Evaluation program (BIAevaluation 3.1, ~~Biacore~~BIACORE) was used for data analysis. The soluble analyte (40 µl at various concentrations) was injected at a flow rate of 20 µl/min in HBS buffer, on dextran layers containing

500 or 540 reflectance units (RU), and 1000 or 700 RU of KIR2DL1 and KIR2DL3, respectively. Data are representative of 6 independent experiments. The results are shown in Table 1, below.

Table 1. ~~BIAcore~~ BIACORE analysis of DF200 mAb binding to immobilized KIR2DL1 and KIR2DL3.

Please substitute the following paragraph on page 82, beginning at line 1:

The present invention relates to novel antibody compositions ~~and methods~~ for regulating an immune response in a subject. More particularly, the invention relates to specific antibodies that regulate the activity of NK cells and allow a potentiation of NK cell cytotoxicity in mammalian subjects. The invention also relates to fragments and derivatives of such antibodies, as well as pharmaceutical compositions comprising the same and their uses, particularly in therapy, to increase NK cell activity or cytotoxicity in subjects.